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1600

RAW SEQUENCE LISTING

DATE: 03/13/2003

PATENT APPLICATION: US/09/910,186B

TIME: 15:08:51

Input Set : A:\09910186SubSeqList.txt

Output Set: N:\CRF4\03132003\I910186B.raw

```

1 <110> APPLICANT: Smith, Leonard A.
2   Byrne, Michael P.
3   Middlebrook, John L.
4   Lapenotiere, Hugh
5   Clayton, Michael A.
6   Brown, Douglas R.
8 <120> TITLE OF INVENTION: RECOMBINANT VACCINE AGAINST BOTULINUM
9   NEUROTOXIN
11 <130> FILE REFERENCE: A33626-A 067252.0107
C--> 13 <140> CURRENT APPLICATION NUMBER: US/09/910,186B
C--> 14 <141> CURRENT FILING DATE: 2001-07-20
16 <150> PRIOR APPLICATION NUMBER: PCT/US00/12890
17 <151> PRIOR FILING DATE: 2000-05-12
19 <150> PRIOR APPLICATION NUMBER: 60/133,865
20 <151> PRIOR FILING DATE: 1999-05-12
22 <150> PRIOR APPLICATION NUMBER: 60/133,866
23 <151> PRIOR FILING DATE: 1999-05-12
25 <150> PRIOR APPLICATION NUMBER: 60/133,867
26 <151> PRIOR FILING DATE: 1999-05-12
28 <150> PRIOR APPLICATION NUMBER: 60/133,868
29 <151> PRIOR FILING DATE: 1999-05-12
31 <150> PRIOR APPLICATION NUMBER: 60/133,869
32 <151> PRIOR FILING DATE: 1999-05-12
34 <150> PRIOR APPLICATION NUMBER: 60/146,192
35 <151> PRIOR FILING DATE: 1999-07-29
37 <160> NUMBER OF SEQ ID NOS: 42
39 <170> SOFTWARE: FastSEQ for Windows Version 4.0
41 <210> SEQ ID NO: 1
42 <211> LENGTH: 1332
43 <212> TYPE: DNA
44 <213> ORGANISM: Artificial Sequence
46 <220> FEATURE:
47 <223> OTHER INFORMATION: Synthetic construct based on BoNTA Hc
W--> 49 <221> NAME/KEY: CDS
50 <222> LOCATION: (13)...(1326)
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53 gaattcgaaa cg atg cgt ctg ctg tct acc ttc act gaa tac atc aag aac 51
54   Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn
55   1 5 10
57 atc atc aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg 99
58 Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu
59 15 20 25
61 atc gac ctg tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt 147

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62 Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val
63 30 35 40 45
65 aac ttc gat ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa 195
66 Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu
67 50 55 60
69 tct tcc aaa atc gaa gtt atc ctg aag aat gct atc gta tac aac tct 243
70 Ser Ser Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser
71 65 70 75
73 atg tac gaa aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac 291
74 Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr
75 80 85 90
77 ttc aac tcc atc tct ctg aac aat gaa tac acc atc atc aac tgc atg 339
78 Phe Asn Ser Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met
79 95 100 105
81 gaa aac aat tct ggt tgg aaa gta tct ctg aac tac ggt gaa atc atc 387
82 Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile
83 110 115 120 125
85 tgg act ctg cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa 435
86 Trp Thr Leu Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys
87 130 135 140
89 tac tct cag atg atc aac atc tct gac tac atc aat cgc tgg atc ttc 483
90 Tyr Ser Gln Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe
91 145 150 155
93 gtt acc atc acc aac aat cgt ctg aat aac tcc aaa atc tac atc aac 531
94 Val Thr Ile Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn
95 160 165 170
97 ggc cgt ctg atc gac cag aaa ccg atc tcc aat ctg ggt aac atc cac 579
98 Gly Arg Leu Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His
99 175 180 185
101 gct tct aat aac atc atg ttc aaa ctg gac ggt tgt cgt gac act cac 627
102 Ala Ser Asn Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His
103 190 195 200 205
105 cgc tac atc tgg atc aaa tac ttc aat ctg ttc gac aaa gaa ctg aac 675
106 Arg Tyr Ile Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn
107 210 215 220
109 gaa aaa gaa atc aaa gac ctg tac gac aac cag tcc aat tct ggt atc 723
110 Glu Lys Glu Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile
111 225 230 235
113 ctg aaa gac ttc tgg ggt gac tac ctg cag tac gac aaa ccg tac tac 771
114 Leu Lys Asp Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr
115 240 245 250
117 atg ctg aat ctg tac gat ccg aac aaa tac gtt gac gtc aac aat gta 819
118 Met Leu Asn Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val
119 255 260 265
121 ggt atc cgc ggt tac atg tac ctg aaa ggt ccg cgt ggt tct gtt atg 867
122 Gly Ile Arg Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met
123 270 275 280 285
125 act acc aac atc tac ctg aac tct tcc ctg tac cgt ggt acc aaa ttc 915
126 Thr Thr Asn Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe

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127          290          295          300
129 atc atc aag aaa tac gcg tct ggt aac aag gac aat atc gtt cgc aac 963
130 Ile Ile Lys Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn
131          305          310          315
133 aat gat cgt gta tac atc aat gtt gta gtt aag aac aaa gaa tac cgt 1011
134 Asn Asp Arg Val Tyr Ile Asn Val Val Val Lys Asn Lys Glu Tyr Arg
135          320          325          330
137 ctg gct acc aat gct tct cag gct ggt gta gaa aag atc ttg tct gct 1059
138 Leu Ala Thr Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala
139          335          340          345
141 ctg gaa atc ccg gac gtt ggt aat ctg tct cag gta gtt gta atg aaa 1107
142 Leu Glu Ile Pro Asp Val Gly Asn Leu Ser Gln Val Val Val Met Lys
143 350          355          360          365
145 tcc aag aac gac cag ggt atc act aac aaa tgc aaa atg aat ctg cag 1155
146 Ser Lys Asn Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln
147          370          375          380
149 gac aac aat ggt aac gat atc ggt ttc atc ggt ttc cac cag ttc aac 1203
150 Asp Asn Asn Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn
151          385          390          395
153 aat atc gct aaa ctg gtt gct tcc aac tgg tac aat cgt cag atc gaa 1251
154 Asn Ile Ala Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu
155          400          405          410
157 cgt tcc tct cgc act ctg ggt tgc tct tgg gag ttc atc ccg gtt gat 1299
158 Arg Ser Ser Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp
159          415          420          425
161 gac ggt tgg ggt gaa cgt ccg ctg taa gaattc 1332
162 Asp Gly Trp Gly Glu Arg Pro Leu *
163 430          435
166 <210> SEQ ID NO: 2
167 <211> LENGTH: 437
168 <212> TYPE: PRT
169 <213> ORGANISM: Artificial Sequence
171 <220> FEATURE:
172 <223> OTHER INFORMATION: Encoded polypeptide of a synthetic construct based
173 on BoNTA Hc
175 <400> SEQUENCE: 2
176 Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn
177 1 5 10 15
178 Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
179 20 25 30
180 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
181 35 40 45
182 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
183 50 55 60
184 Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
185 65 70 75 80
186 Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
187 85 90 95
188 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn

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189          100          105          110
190 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
191          115          120          125
192 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
193          130          135          140
194 Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
195 145          150          155          160
196 Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu
197          165          170          175
198 Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
199          180          185          190
200 Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile
201          195          200          205
202 Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
203          210          215          220
204 Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
205 225          230          235          240
206 Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn
207          245          250          255
208 Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg
209          260          265          270
210 Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn
211          275          280          285
212 Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys
213          290          295          300
214 Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg
215 305          310          315          320
216 Val Tyr Ile Asn Val Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr
217          325          330          335
218 Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile
219          340          345          350
220 Pro Asp Val Gly Asn Leu Ser Gln Val Val Val Met Lys Ser Lys Asn
221          355          360          365
222 Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn
223          370          375          380
224 Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala
225 385          390          395          400
226 Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser
227          405          410          415
228 Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp
229          420          425          430
230 Gly Glu Arg Pro Leu
231          435
234 <210> SEQ ID NO: 3
235 <211> LENGTH: 1323
236 <212> TYPE: DNA
237 <213> ORGANISM: Artificial Sequence
239 <220> FEATURE:
240 <223> OTHER INFORMATION: Synthetic construct based on BoNTA Hc

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Input Set : A:\09910186SubSeqList.txt

Output Set: N:\CRF4\03132003\I910186B.raw

W--> 242 <221> NAME/KEY: CDS

243 <222> LOCATION: (13)...(1314)

W--> 245 <400> 3

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246 gaattcgaac cg atg tct acc ttc act gaa tac atc aag aac atc atc aat 51
247           Met Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn
248           1           5           10
250 acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg atc gac ctg 99
251 Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
252           15           20           25
254 tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt aac ttc gat 147
255 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
256           30           35           40           45
258 ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa tct tcc aaa 195
259 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
260           50           55           60
262 atc gaa gtt atc ctg aag aat gct atc gta tac aac tct atg tac gaa 243
263 Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
264           65           70           75
266 aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac ttc aac tcc 291
267 Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
268           80           85           90
270 atc tct ctg aac aat gaa tac acc atc atc aac tgc atg gaa aac aat 339
271 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
272           95           100          105
274 tct ggt tgg aaa gta tct ctg aac tac ggt gaa atc atc tgg act ctg 387
275 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
276 110           115          120          125
278 cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa tac tct cag 435
279 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
280           130          135          140
282 atg atc aac atc tct gac tac atc aat cgc tgg atc ttc gtt acc atc 483
283 Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
284           145          150          155
286 acc aac aat cgt ctg aat aac tcc aaa atc tac atc aac ggc cgt ctg 531
287 Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu
288           160          165          170
290 atc gac cag aaa ccg atc tcc aat ctg ggt aac atc cac gct tct aat 579
291 Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
292           175          180          185
294 aac atc atg ttc aaa ctg gac ggt tgt cgt gac act cac cgc tac atc 627
295 Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile
296 190           195          200          205
298 tgg atc aaa tac ttc aat ctg ttc gac aaa gaa ctg aac gaa aaa gaa 675
299 Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
300           210          215          220
302 atc aaa gac ctg tac gac aac cag tcc aat tct ggt atc ctg aaa gac 723
303 Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
304           225          230          235
306 ttc tgg ggt gac tac ctg cag tac gac aaa ccg tac tac atg ctg aat 771

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VERIFICATION SUMMARY

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Input Set : A:\09910186SubSeqList.txt

Output Set: N:\CRF4\03132003\I910186B.raw

L:13 M:270 C: Current Application Number differs, Replaced Current Application Number
L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:49 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:52 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:242 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:245 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:435 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:438 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:5
L:628 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:631 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:7
L:821 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:824 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:9
L:1020 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1023 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:11
L:1219 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1222 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:13
L:1419 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1422 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:15
L:1610 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1613 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:17
L:1809 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1812 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:19
L:1990 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1993 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:21
L:2171 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2174 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:23
L:2347 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2350 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:25
L:2522 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2525 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:27
L:2692 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2695 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:29
L:2873 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:2876 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:31
L:3054 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3057 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:33
L:3245 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3248 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:35
L:3432 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3435 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:37
L:3617 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:3620 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:39